Remarks

Claims 1, 3, 4, 20, 26, 27, 45, and 58 are amended herein. Claims 2, 21-23, 29-33, 36-44 and 48-55 are canceled herein, without prejudice to renewal. New claims 59-68 are added.

Support for the amendment of claims 1, 3, 4, 20 and 27 can be found throughout the specification, for example at page 5, lines 31-33, page 17, lines 1-10, page 24, lines 3-9, pages 28-30 (such as page 28, lines 31-33, page 33, lines 16-24). Claim 16 is amended to depend from claim 3. Claim 17 is amended to depend from claim 4. Claim 26 is amended as suggested in the Office action; support for this amendment can be found throughout the specification such as on page 28, lines 19-21. Support for the amendment of claim 45 can be found throughout the specification, such as on page 24, lines 9-12, page 27, lines 13-16, page 33, lines 20-24, page 38, lines 28-34. Claim 45 is also amended to correct dependency. Support for the amendment of claim 58 can be found throughout the specification, for example at page 22, line 18 to page 23, line 14.

Support for new claims 59-63 can be found throughout the specification, for example at page 19, line 4 to page 20, line 32, page 24, line 26 to page 27, line 16 and page 39, lines 1-12. Support for new claim 64-68 can be found throughout the specification, for example at page 5, lines 31-33, page 17, lines 1-10, page 24, lines 3-9, pages 28-30.

Applicants believe no new matter is added. Reconsideration of the subject application is respectfully requested.

Priority Claim

Applicants thank Examiner Rawlings for confirming that the priority claim has been perfected.

The Office action asserts that the present claims are not entitled to the filing date of U.S. Provisional Application No. 60/143,560, as allegedly this provisional application does not disclose the amino acid sequence set forth as SEQ ID NO: 14 or the nucleic acid sequence set forth as SEQ ID NO: 13. Applicants respectfully disagree with this assertion. As discussed with Examiner Rawlings, the amino acid sequence set forth as SEQ ID NO: 14 and the nucleic acid sequence set forth as SEQ ID NO: 13 are shown in FIG. 5 of U.S. Provisional Application No. 60/143,560. In view of this information, reconsideration is respectfully requested.

Formal Matters

Applicants acknowledge that the election of Group I drawn to the amino acid sequence set forth as SEQ ID NO: 14 or immunogeneic fragments thereof, nucleic acid encoding these polypeptides, vectors, and methods for eliciting an immune response in a subject, with traverse, has been entered. Applicants believe that the present amendment meets the requirements of 37 C.F.R. § 1.121. The non-elected claims are canceled herein in response to the restriction requirement.

Declaration and Telephone Conference

Applicants thank the Examiner for considering the Declaration of Drs. Pastan and Berzofsky under 37 C.F.R. § 1.132. Applicants also thank Examiner Rawlings for the telephone conference of April 12, 2005, wherein the Office action was discussed. Applicants have made every effort to comply with Examiner Rawlings' suggestions in this amendment. If any matters remain to be addressed before the issuance of a Notice of Allowance, the Applicants respectfully request that the Examiner contact their undersigned representative at the telephone number below for an additional interview.

Objections to the Specification

The specification is objected to for not referring to the full length TARP protein (SEQ ID NO: 14) in the brief description of Fig. 14. The brief description of Fig. 14 is amended herein to refer to SEQ ID NO: 14. Applicants believe that this amendment renders the objection moot.

Rejections Under 35 U.S.C. § 112, first paragraph

Claim 26 was rejected as allegedly including new matter. Applicants respectfully disagree, and submit that the phrase "wherein said subject is a female at risk for developing breast cancer" is supported by the specification for the reasons of record. However, solely to advance prosecution, claim 26 is amended herein to recite "wherein the composition is administered to a female subject to provide an immune defense in the event that a TARP-expressing breast cancer later develops in the female," as requested in the Office action, and as discussed in the telephone conference with Examiner Rawlings.

Claims 1, 3, 4, 6, 10, 15, 17, 20, 24-28, 34, 35, 37, 56 and 57 were rejected as allegedly the specification does not provide sufficient written description for the claimed subject matter. Applicants respectfully disagree with this assertion.

With regard to amino acid sequences at least 90% identical to SEQ ID NO: 14, Applicants respectfully assert that the specification provides adequate written description for the polypeptides for the reasons of record. However, solely to advance prosecution, the claims have been amended so they no longer encompass polypeptides having at least 90% homology to SEQ ID NO: 14. Applicants reserve the right to prosecute this subject matter in a continuation application.

With regard to fragments of TARP of between 8 to 10 amino acids in length, Applicants believe that the specification clearly provides written description of these peptides. SEQ ID NO: 14 is only 58 amino acids in length. Functional domains of SEQ ID NO: 14 are disclosed in Fig. 14. In addition, the claimed epitopes are clearly described in the specification. For example, the specification discloses that epitopes of at least 10 consecutive amino acids, and epitopes that are 8-10 amino acids in length and have anchoring residues (see for example, page 17, lines 1-10, page 24, lines 3-9, pages 28-30, page 33, lines 16-24). Specific configurations of use are disclosed, such as wherein the TARP polypeptide is 9 or 10 amino acids in length and has a leucine or methionine in the second position and valine or leucine in the last positions, and bind HLA-A2 (for example, see page 28, lines 31-33). In addition, biological methods of testing whether an epitope is immunogenic is also provided (for example, see page 17, lines 3-12 and page 30). Computer based programs for predicting MHC binding motifs (immunogenic epitopes) were well known to those of skill in the art at the time the provisional application was filed. For example, TEPITOPE (Sturniolo et al., *Nat. Biotechnol.* 17:555-561, June, 1999) was a matrix based computer program available at the time the application was filed that was used successfully in locating T cell epitopes in several antigens (see Manici et al., *J. Exp. Med.* 189(5):871-9, March 1999). Additional programs were also available at the time the provisional applications were filed. For example, Brusic et al. (*Bioinformatics* 14(2):121-130, 1998) discloses a program (PERUN) that combines a high accuracy of predictions with the ability to integrate new data. Thus, given the knowledge of one of skill in the art, and the clear guidance

provided by the specification, Applicants submit that there is sufficient written description for the claimed polypeptides.

Solely to advance prosecution, claim 3 is amended herein to be directed to polypeptides consisting of eight to ten consecutive amino acids of the amino acid sequence as set forth as SEQ ID NO: 14 (which is 58 amino acids in length), wherein the polypeptide has a leucine or a methionine at the second position and valine or leucine in the last position, and wherein the polypeptide specifically binds HLA-A2. TARP (SEQ ID NO: 14) is only 58 amino acids in length. As discussed with Examiner Rawlings, support for these polypeptides is provided throughout the specification, for example at page 2, lines 15-29, page 17, lines 1-10, page 28, line 1 to page 29, line 29.

The declaration of Drs. Pastan and Berzofsky under 37 C.F.R. § 1.132 (submitted on November 11, 2004) documents that using the information provided in the specification, functional epitopes of TARP having these specific characteristics were readily produced using methods known and available to those of skill in the art.

Claim 4 is amended herein to be directed to the polypeptide including the immunogenic epitope of TARP and a second peptide moiety. As discussed with Examiner Rawlings, support for these polypeptides can be found throughout the specification, for example on page 33, lines 16-24, page 29, lines 4-7, page 27, lines 13-16, and page 24, lines 3-9. Applicants submit that the specification provides sufficient written description for the claims as amended. Applicants note that the Office action, at page 14, states that adequate written description is provided for polypeptides consisting of an immunogenic fragment of eight to ten consecutive amino acids of SEQ ID NO: 14.

Every attempt has been made to comply with the amendments requested in the Office action (see the last paragraph of page 14 to the first line of page 15 of the Office action dated February 16, 2005) and to place the claims in proper form, as discussed in the telephone conference of April 12, 2005.

Reconsideration and withdrawal of the rejection are respectfully requested. In the unlikely event that this rejection is maintained, the Examiner is respectfully requested to contact the undersigned for a telephone interview.

Claims 1, 3, 4, 6, 10, 15, 17, 20, 24-28, 34-35, 47, and 56-58 were rejected under 35 U.S.C. § 112, first paragraph as allegedly not being enabled by the specification. Applicants respectfully disagree with this rejection.

The Office action alleges that it would require undue experimentation to make and use the claimed polypeptides. Specifically, the Office action asserts that because only two of the four polypeptides that have a leucine or a methionine at the second position and valine or leucine in the last position actually bound MHC, it must require undue experimentation to select the polypeptides that bind MHC. Applicants respectfully disagree with the assertion as applied to the claims as amended.

As demonstrated in the Declaration of Drs. Pastan and Berzofsky under 36 CFR § 1.132, one of skill in the art can readily identify polypeptide sequences of interest. Moreover, one of skill in the art can use assays well known in the art to determine that the claimed polypeptides bind MHC, as documented in the Declaration of Drs. Pastan and Berzofsky under 36 CFR § 1.132. This Declaration describes the use of assays to determine that TARP 27-35 and TARP29-37 have measurable binding to HLA-A2. The Office action asserts that as Oh et al. (*Cancer Res.* 64:2610-2618, 2004, already of record) discloses that TARP27-35 had higher binding than TARP29-37 and that TARP29-37 induces CD8+ cells, but that TARP 29-37 did not induce CD8+ cells, as evidence that the specification cannot be enabling for all TARP peptides that bind MHC.

Applicants would like to call the Examiner's attention to the disclosure of Oh et al. at page 2612. This page does disclose that TARP29-37 and TARP 27-35 have measurable binding to HLA-A2 (and that TARP2-9 and TARP22-30 did not have measurable binding). However, Oh et al. also discloses that:

> "the theoretical half-life of peptide binding to HLA-A2 molecules was also predicted based on running the software program for peptide motif search and the results were consistent with the data...." (see page 2612, column 1, last three lines of the first paragraph).

TARP 29-37, predicted to have the highest binding affinity, bound HLA-A2 with the highest affinity (see Fig. 1 of Oh et al.). TARP29-37 also induced an immune response (see Fig. 2 and the Declaration of Drs. Pastan and Berzofsky under 36 CFR § 1.132, paragraph 5). Thus, Applicants submit that one of skill in the art could readily identify peptides of use.

Applicants respectfully disagree with the assertion that the claimed peptides cannot be made without the need for undue experimentation. As documented by the Declaration of Drs. Pastan and Berzofsky under 36 CFR § 1.132, and as discussed above, the claimed peptides have been produced and have been shown to induce an immune response. Applicants submit that it is clear that the direction of the specification clearly provided sufficient guidance to produce polypeptides having an amino acid set forth as SEQ ID NO: 14, and polypeptides that were eight to ten amino acids in length of SEQ ID NO: 14 that bound HLA-A2. Using the guidance provided by the specification, these polypeptides were shown to be of use in inducing an immune response.

The eight factors to be considered in determining whether undue experimentation would be required are provided by *In re Wands*, 858 F.2d 731 (*Fed. Cir. 1988*): (1) the quantity of experimentation necessary, (2) the amount of direction provided, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of one in the art, (7) the predicatability of the art, and (8) the breadth of the claims.

In the present case, as documented by the Declaration of Drs. Pastan and Berzofsky under 36 CFR § 1.132: (1) undue experimentation is not necessary, (2) sufficient direction is provided by the specification, (3) there are working examples (4) the nature of the invention is clear (5) the prior art teaches methods of use in identifying immunogenic epitopes and methods for using polypeptides to produce an immune response (but does not teach SEQ ID NO: 14, immunogenic epitopes of SEQ ID NO: 14, specific uses of the claimed polypeptides) (6) the skill of one in the art is high, (7) given the guidance provided by the specification one of skill in the art can make and use the claimed polypeptides, and (8) the breadth of the amended claims is fully supported by the specification. Thus, Applicants respectfully submit that the claims are fully enabled by the specification.

With regard to Wolfgang et al., Applicants do not deny that this paper states that "it is not yet possible to establish the role of TARP in prostate cancer." Once again, the full quote is copied below:

> "On the basis of the current results, it is not yet possible to establish the role of TARP in prostate cancer cell growth or normal cell growth. *However, the results presented in this paper propose a pathway that links TARP expression to the modulation*

of genes involved in generating a malignant phenotype in prostate cancer cells. The question that remains is, what are the downstream components..." [emphasis added].

Wolfgang et al. discloses that expression of TARP in prostate cancer cells lead to increased growth rate (see the title and abstract). Wolfgang et al. concludes that "These results suggest that TARP has a role in regulating growth and gene expression in prostate cancer cells" (see the last line of the abstract). However, Wolfgang et al. admits that all the downstream elements in the pathway between TARP expression and cancer are not known.

The argument presented in the Office action seems to assert that unless every element in a molecular pathway is known, any patent application cannot be enabling for a polypeptide or a chemical compound of use to treat cancer. This clearly is not the position of the U.S. PTO: if every downstream effect of every chemical compound or polypeptide were required to enable a claim to treatment or inducing an immune response then no patents would ever issue that include claims to chemotherapeutic compounds or immunosuppressive agents. The elucidation of downstream biochemical pathways that occur endogenously in a cell upon treatment with an agent of interest is not the standard required to enable claims to the use of specific agents.

Data has been presented documenting that the claimed polypeptides can be produced, documenting that TARP is expressed in specific cancers, and demonstrating that the claimed polypeptides can be used to induce an immune response. The specification provides considerable direction and guidance as to how to identify fragments of eight to ten amino acids of SEQ ID NO: 14 that bind HLA-A2, and the use of these polypeptides to induce an immune response. Thus, based on the evidence of record, Applicants submit that the claims are enabled.

Applicants note that the specification discloses that prostate and breast cancer can be detected by assessing the expression of TARP (see page 6, lines 19-32, page 50, lines 10-15, page 59, lines 25-28 and page 60, lines 8-15). Oh et al. documents that TARP is expressed in a large number of prostate cancers (see page 2610, column 2, first paragraph, last two lines). As discussed with Examiner Rawlings, Applicants submit that this demonstrates an immediate, well established utility for the claimed polypeptides. This supports the assertion that the claims are fully enabled by the specification.

Reconsideration and withdrawal of the rejection are respectfully requested.

Claims Objections

Claim 45 is objected to as not differing in scope from claim 2. Applicants submit that the amendment of claim 45 renders this rejection moot.

Claim 58 was objected to for being drawn to a non-elected invention, and for a formatting error. Applicants submit that the amendment of claim 58 renders the objections moot.

Conclusion

Applicants believe that the claims are in condition for allowance, which action is respectfully requested. If for any reason a further Office action will be issued (and not a Notice of Allowance), the Applicants respectfully request that Examiner Rawlings contact their undersigned representative for a telephone interview.

Respectfully submitted,

KLARQUIST SPARKMAN, LLP

By _____
Susan Alpert Siegel, Ph.D.
Registration No. 43,121

One World Trade Center, Suite 1600
121 S.W. Salmon Street
Portland, Oregon 97204
Telephone: (503) 595-5300
Facsimile: (503) 228-9446